Sjogren's syndrome

Meijer, Jiska Marianne

Jiska M Meijer*[1], Petra M Meiners*[1], James JR Huddleston Slater[1,2,] Fred KL Spijkervet[1], Cees GM Kallenberg[3], Arjan Vissink[1], Hendrika Bootsma[3]

* These authors contributed equally to this paper

Rheumatology. 2009 Sep;48(9):1077-82

Chapter 2

Health related quality of life, employment and disability in patients with Sjögren's syndrome

[1] Departments of Oral and Maxillofacial Surgery, [2] Oral Health Care and Clinical Epidemiology, Academic Center for Oral Health, [3] Rheumatology and Clinical Immunology, University Medical Center Groningen, University of Groningen, The Netherlands

Abstract

Objective To compare health related quality of life (HR-QOL), employment and disability between primary (pSS) and secondary (sSS) Sjögren's syndrome (SS) patients and the general Dutch population.

Methods HR-QOL, employment and disability were assessed in SS patients regularly attending the University Medical Center Groningen (n=235). HR-QOL, employment and disability were evaluated with the Short Form-36 questionnaire (SF-36) and an employment and disability questionnaire. Results were compared with Dutch population data (matched for sex and age). Demographical and clinical data associated with HR-QOL, employment and disability were assessed.

Results Response rate was 83%. SS patients scored lower on HR-QOL than the general Dutch population. sSS patients scored lower on physical functioning, bodily pain and general health than pSS patients. Predictors for reduced HR-QOL were fatigue, tendomyalgia, articular involvement, use of artificial saliva, use of antidepressants, comorbidity, male sex, and eligibility for disability compensation (DC). Employment was lower and DC rates were higher in SS patients compared with the Dutch population.

Conclusions SS has a large impact on HR-QOL, employment and disability.

Introduction

Sjögren's syndrome (SS) is a chronic, systemic, lymphoproliferative autoimmune disease affecting the exocrine glands.(1) The salivary and lachrymal glands are most commonly affected, resulting in dry mouth and dry eyes. Extraglandular involvement can occur in SS, and includes, amongst others, pulmonary disease, renal disease and vasculitis. Moreover, almost all patients suffer from fatigue. SS can be primary (pSS) or secondary (sSS), the latter being associated with other autoimmune diseases such as rheumatoid arthritis (RA) or systemic lupus erythematosus (SLE). The estimated prevalence of SS in the general population is between 0.5-2%, which makes SS, after RA, the most common systemic autoimmune disease. (2;3)

Rheumatologic conditions have a major impact on patients. Apart from the symptoms mentioned above, patients may be restricted in their activities and their participation in society, resulting in a reduced health related quality of life (HR-QOL) and an impaired socioeconomic status. The latter may result in lower employment rates and more disability as compared with the general population.(4)

SS is known to affect patients' physical, psychological and social functioning (5), but the impact of SS on HR-QOL, and especially on employment and disability, has not been studied extensively. Studies available were either performed in small series of SS patients (6;7) or mainly aimed at comparison with other rheumatic diseases (6-9), fatigue (9) and psychological status (8), or at developing new tools for measuring fatigue and general discomfort in pSS patients.(10) Comparison between pSS and sSS has occasionally been described for HR-QOL (7;9), but not for employment and disability. The aim of this study was, therefore, to evaluate HR-QOL, employment and disability in a large cohort of Dutch SS patients, to relate outcomes to clinical and demographic data in this patient cohort, and to compare these data with those available for the general Dutch population. In addition, HR-QOL, employment and disability were compared between pSS and sSS patients, since it was hypothesized that the disease burden of sSS might differ from that of pSS due to co-existing autoimmune disease(s).

Patients and methods

Patients

SS patients (185 pSS, 50 sSS) regularly attending the departments of Rheumatology, Clinical Immunology and Oral and Maxillofacial Surgery of the University Medical Center Groningen (UMCG), The Netherlands, were enrolled in this study. All patients were above the age of 18 years and fulfilled the European-American criteria for SS.(11) All patients participating in this study were followed according to protocol, and, therefore, data on extraglandular manifestations (EGM) were available for all patients. Ethical approval for this study was obtained from the local Institutional Review Board.

Methods

Demographical and clinical data were obtained by chart review. EGM were defined in accordance with previous studies.(12;13) Tendomyalgia, skin involvement other than cutaneous vasculitis, oesophageal involvement, bladder involvement and thrombocytopenia are commonly observed symptoms and signs, and, thus, were also considered as EGM. Moreover, at every visit the rheumatologists systematically evaluated the presence of EGMs.

Questionnaires were sent by regular mail to all patients. Six weeks after sending the questionnaires, patients who had not responded were approached by phone once, to ask for participation.

In the first questionnaire, patients were asked whether they suffered from arthralgia and/or tendomyalgia, fatigue, dry mouth and dry eyes. In addition, it was asked which symptom they considered to be their most severe complaint.

To evaluate HR-QOL, a validated Dutch translation of the Short Form 36 (SF-36) was used.(12;14) The SF-36 is a questionnaire consisting of 36 items, with eight scales assessing two dimensions, viz. physical and mental health functioning. Scales and summary scores vary from 0 to 100, with 0 being the worst possible health status and 100 representing the best possible health status.

The third questionnaire focused on level of education, employment and disability. In The Netherlands, an individual who is judged to be impaired by at least 80% is entitled to full disability compensation (DC). Individuals impaired by 15-80% are entitled to partial DC.

Age and sex matched data for the general Dutch population on the SF-36 were obtained from Aaronson et al.(14) Data regarding employment and DC were obtained from the Dutch Office of Statistics (Centraal Bureau voor Statistiek, CBS, Voorburg, The Netherlands).

Statistical analysis

The T-tests and χ^2 tests were used for the comparison of demographical data, HR-QOL, employment and receiving DC between responders and non-responders, between pSS and sSS patients, and between SS patients and the general Dutch population. Alpha was set at 5%. Correlation between disease duration and HR-QOL was evaluated with a Pearson correlation test.

To create effect models, univariate analyses were performed for each predictor variable on the outcomes (HR-QOL, employment and receiving DC). If variables were found to be significant, *P*-values were used in the further development of the model. Predictors with a *P*-value less than or equal to 0.2 were simultaneously entered into a multivariable model, after which backward elimination of predictors was used to remove non-significant

Table I Patients' characteristics.

Characteristics	All responding SS patients (n=195)	pSS (n=154)	sSS (n=41)	*P* pSS vs sSS
Age (years; mean±SD)	55.5±15.0	54.6±15.1	58.9±14.2	0.103
Age at diagnosis (years; mean±SD)	45.7±15.7	45.5±15.3	46.5±17.1	0.715
Female sex (n, %)	179 (91.8%)	143 (92.9%)	36 (87.8%)	0.197
Partner (n, %)	153 (78.5%)	121 (78.6%)	32 (78.0%)	0.769
Disease duration (years; mean±SD)	9.7±8.8	9.0±8.0	12.5±11.0	0.121
Immunological features				
Focus score (mean±SD)	2.7±1.8	2.7±2.0	2.5±2.0	0.716
ANA (n, %)	189 (96.9%)	151 (98.1%)	38 (92.7%)	0.109
Anti-Ro/SS-A (n, %)	155 (79.5%)	129 (83.8%)	26 (63.4%)	0.014
Anti-La/SS-B (n, %)	107 (54.9%)	90 (58.4%)	17 (41.5%)	0.077
IgG (g/L ; mean±SD)	18.6±7.2	18.8±6.8	17.7±8.3	0.405
IgA (g/L; mean±SD)	2.8±1.3	2.7±1.2	3.2±1.5	0.023
IgM (g/L; mean±SD)	1.4±1.0	1.4±1.1	1.3±0.8	0.629
RF (kIU/L; mean±SD)	106.2±190.2	99.5±195.6	131.2±168.7	0.343
Second auto immune disease (n, %)				
none	154 (79.0%)	154 (100%)	-	-
SLE	19 (9.7%)	-	19 (46.3%)	-
RA	16 (8.2%)	-	16 (39.0%)	-
Other	6 (3.1%)	-	6 (14.6%)	-
Extraglandular manifestations (n, %)	185 (94.9%)	144 (93.5%)	41 (100%)	0.112
Articular involvement*	110 (56.4%)	80 (51.9%)	30 (73.2%)	0.017
Raynaud's phenomenon	84 (43.1%)	67 (43.5%)	17 (41.5%)	0.789
Tendomyalgia	80 (41.0%)	64 (41.6%)	16 (39.0%)	0.746
Pulmonary involvement	33 (16.9%)	25 (16.2%)	8 (19.5%)	0.631
Lymphoproliferative disease	30 (15.4%)	24 (15.6%)	6 (14.6%)	0.869
Cutaneous vasculitis	28 (14.4%)	22 (14.3%)	6 (14.6%)	0.967
Peripheral neuropathy	26 (13.3%)	20 (13.0%)	6 (14.6%)	0.794
Skin involvement other than cutaneous vasculitis*	22 (11.3%)	13 (8.4%)	9 (22.0%)	0.047
Bladder involvement	22 (11.3%)	18 (11.7%)	4 (9.8%)	0.719
Lymphadenopathy	21 (10.8%)	19 (12.3%)	2 (4.9%)	0.168
Renal involvement	19 (9.7%)	14 (9.1%)	5 (12.2%)	0.560
Autoimmune thyroiditis	19 (9.7%)	16 (10.4%)	3 (7.3%)	0.548
Autoimmune hepatitis	12 (6.2%)	11 (7.1%)	1 (2.4%)	0.262
Oesophageal involvement	9 (4.6%)	7 (4.5%)	2 (4.9%)	0.872
Fever	8 (4.1%)	7 (4.5%)	1 (2.4%)	0.541
Serositis	6 (3.1%)	5 (3.2%)	1 (2.4%)	0.785
Myositis	5 (2.6%)	3 (1.9%)	2 (4.9%)	0.295
CNS involvement	5 (2.6%)	5 (3.2%)	-	0.241
Thrombocytopenia	2 (1.0%)	2 (1.3%)	-	0.337
Acute pancreatitis	1 (0.5%)	1 (0.6%)	-	-

This table continues on the next page.

Table 1 Patients' characteristics, continued.

Characteristics	All responding SS patients (n=195)	pSS (n=154)	sSS (n=41)	*P* pSS vs sSS
Comorbidity (n, %)**	75 (38.5%)	59 (38.3%)	16 (39.0%)	0.957
Osteoarthritis	15 (7.7%)	13 (8.4%)	2 (4.9%)	-
Cardiovascular disease	13 (6.7%)	9 (5.8%)	4 (9.8%)	-
Neurologic disease	10 (5.1%)	9 (5.8%)	1 (2.4%)	-
Diabetes mellitus	8 (4.1%)	5 (3.2%)	3 (7.3%)	-
Pulmonary disease	7 (3.6%)	5 (3.2%)	2 (4.9%)	-
Gastro-intestinal disease	6 (3.1%)	5 (3.2%)	1 (2.4%)	-
Eye disease	5 (2.6%)	4 (2.6%)	1 (2.4%)	-
Malignancy	3 (1.5%)	3 (1.9%)	0	-
Urologic disease	3 (1.5%)	2 (1.0%)	1 (2.4%)	-
Osteoporosis	2 (1.0%)	1 (0.6%)	1 (2.4%)	-
Depression	19 (9.7%)	15 (9.7%)	4 (9.8%)	-
Other	10 (5.2%)	6 (3.9%)	4 (9.8%)	-
Therapy (n, %)				
Artificial tears	151 (77.4%)	119 (77.3%)	32 (78.0%)	0.711
Oral moisturising gel	46 (23.6%)	37 (24.0%)	9 (22.0%)	0.840
Artificial saliva	20 (10.3%)	16 (10.4%)	4 (9.8%)	0.942
Pilocarpine	18 (9.2%)	15 (9.7%)	3 (7.3%)	0.663
NSAIDs	47 (24.1%)	31 (20.1%)	16 (39.0%)	0.012
Antimalarial drugs	31 (15.9%)	20 (13.0%)	11 (26.8%)	0.031
Oral corticosteroids	26 (13.3%)	20 (13.0%)	6 (14.6%)	0.783
Rituximab	20 (10.3%)	19 (12.3%)	1 (2.4%)	0.036
Other immunosuppressives	17 (8.7%)	9 (5.8%)	8 (19.5%)	0.006
Antidepressants	18 (9.2%)	14 (9.1%)	4 (9.8%)	0.769

n = number of patients; SLE = systemic lupus erythematosus; RA = rheumatoid arthritis; CNS = central nervous system; NSAIDs = non-steroidal anti-inflammatory drugs. *Extraglandular manifestation that affect sSS patients significantly more frequently than pSS patients. **Comorbidity unrelated to SS.

predictors (*P*-value to remove >0.10). Subsequently, predictors not included in the multivariable model were entered to determine whether they could now enter the model, after which the procedure of backward elimination of predictors was repeated. Variables in the final models were tested for possible interactions. All analyses were carried out using SPSS for Windows version 16.0.

Results

Patient characteristics (table 1)

196 patients (180 females, 16 males; mean age at diagnosis: 45.7±15.7 years) responded to the mail survey (83%). One patient returned the questionnaire incompletely and was therefore excluded. The mean age (±SD) at the time of completing the questionnaire was

55.5±15.0 years; the mean disease duration was 9.7±8.8 years. 154 patients (79%) were classified as pSS and 41 patients (21%) as sSS. Demographic data did neither differ between pSS and sSS patients nor between responders and non-responders.

The most frequently associated autoimmune disorders in sSS patients were SLE (46%) and RA (39%). Seventy-five patients (39%) suffered from at least one comorbid condition.

Artificial tears were used by 77% and antidepressants by 9% of patients. Non-steroidal anti-inflammatory drugs, antimalarial drugs and other immuno-suppressants were used more frequently by sSS patients, whereas rituximab was more frequently prescribed in pSS patients.

EGM were present in 185 patients (95%). The main EGM were articular involvement, Raynaud's phenomenon and tendomyalgia. sSS patients suffered from articular- and skin involvement more often than pSS patients. When restricting the EGM to the EGM defined in accordance with previous studies (21;22), EGM occurred in 177 patients (91%; pSS 137; sSS 40).

Current symptoms

Almost all patients suffered from dry mouth (n=183; 94%), dry eyes (n=183; 94%), and fatigue (n=166; 85%). Fatigue was the most severe symptom in 78 patients (40%). Arthralgia and/or tendomyalgia was present in 148 patients (76%). The prevalence of sicca symptoms, fatigue and arthralgia and/or tendomyalgia was comparable between pSS and sSS patients.

Health related quality of life

When compared with the general Dutch population, HR-QOL was significantly decreased in SS patients as demonstrated by reduced SF-36 scores on six out of the eight scales and for the summary scores for physical and mental functioning (table 2).

sSS patients experienced a significantly lower HR-QOL than pSS patients on three of the four physical scales (physical functioning, bodily pain and general health), however, no differences were observed on the psychological scales. HR-QOL was comparable between sSS patients with either RA or SLE as the associated autoimmune disorder. Disease duration was not significantly correlated with any of the SF-36 scales. Highly educated patients scored significantly better on physical functioning ($p=0.042$) and mental health ($p=0.005$) compared with non-highly educated patients.

Multivariate regression analysis showed that fatigue, tendomyalgia, comorbidity, male sex and receiving DC were associated with a reduced physical component summary score (PCS) (table 3). Confounders were disease duration, use of NSAIDs and antidepressants and employment. No significant effect modifiers (interaction terms) were found.

Multivariate regression analysis for the mental component summary score (MCS) demonstrated that fatigue, articular involvement, use of artificial saliva, use of antidepressants, and comorbidity were associated with a reduced MCS, whereas dry mouth was associated with a higher MCS (table 3). Receiving DC was a confounding factor for the determinants in the primary model for the MCS. No effect modifiers were found.

Socioeconomic status

135 patients (69%) were of working age (18-65 years) (table 4). SS patients were significantly less often employed ($p<0.001$), worked fewer hours ($p=0.015$) and were less frequently full time employed ($p<0.01$), compared with the Dutch population. In detail, approximately half of the SS patients (n=69) had paid employment. Only seven SS patients (10%) worked full-time (at least 36 hours). On average, SS patients worked 21.7±11.6 hours per week. The mean sick

Table 2 SF-36 scores for SS patients and the general Dutch population.

SF-36 scales and summary scores	GDP Mean (SD) n=195	RSS Mean (SD) n=195	*P* RSS vs GDP	pSS Mean (SD) n=154	sSS Mean (SD) n=41	*P* pSS vs sSS
PF	74.8 (25.8)	59.2 (26.0)	0.000	62.0 (25.1)	48.9 (27.0)	0.004
RP	70.3 (36.3)	41.0 (42.9)	0.000	44.0 (42.7)	29.1 (41.9)	0.058
BP	68.7 (25.6)	64.7 (24.4)	0.136	68.0 (23.0)	52.1 (25.7)	0.000
GH	65.7 (21.5)	40.3 (18.2)	0.000	41.9 (18.4)	34.2 (16.3)	0.018
VT	63.8 (21.0)	45.2 (20.1)	0.000	46.0 (20.4)	42.0 (18.9)	0.266
SF	81.3 (25.6)	63.1 (26.2)	0.000	64.5 (26.6)	57.9 (24.5)	0.152
RE	79.7 (34.4)	70.0 (41.4)	0.005	71.5 (41.5)	63.9 (40.9)	0.324
MH	73.3 (19.0)	70.3 (18.4)	0.055	70.6 (18.9)	69.0 (16.8)	0.627
PCS	73.0 (24.6)	51.7 (23.7)	0.000	53.3 (23.6)	44.7 (23.2)	0.055
MCS	74.5 (21.1)	63.3 (21.2)	0.000	64.0 (21.2)	60.5 (21.4)	0.385

n = number of patients; SF-36 = short form-36; GDP = general Dutch population; RSS = all responding SS patients; pSS primary Sjögren syndrome; sSS = secondary Sjögren syndrome; PF = physical functioning; RP = physical role functioning; BP = bodily pain; GH = general health; VT = vitality; SF = social functioning; RE = emotional role functioning; MH = mental health; PCS = physical component summary score; MCS = mental component summary score.

leave was 15.6±39.0 days during the past year (range 0-192 days). Highly educated patients were significantly more often employed than non-highly educated patients (p=0.001). No differences were found between pSS and sSS patients regarding employment variables.

Sixty-three working age patients (47%) received DC, because they were considered to be (partially) unfit for work (table 4). 28 of these patients (44%) were entitled to full DC. Moreover, 41 of the 63 patients receiving DC (65%) mentioned pSS, sSS or the associated rheumatic disease as the cause of receiving DC. No differences in DC were found between pSS and sSS patients or between highly educated and non-highly educated patients. A significantly higher percentage of SS patients received DC (47%) when compared with the general Dutch population (2%).

Multivariate regression analysis for employment (table 5) showed that a high level of education was associated with employment. Bladder involvement, use of oral moisturizing gel, NSAIDs and oral corticosteroids, comorbidity and age at diagnosis were all negatively associated with employment. Autoimmune thyroiditis, use of artificial tears and age were confounding factors for these determinants. No interaction terms were found. Multivariate regression analysis for receiving DC (table 5) demonstrated that the number of EGM, use of artificial saliva and antimalarial drugs, comorbidity, high level of education, and male sex were associated with receiving DC. Age at diagnosis was negatively associated with receiving DC. Fatigue, skin involvement other than cutaneous vasculitis and use of pilocarpine were confounding factors for the determinants in the primary model for receiving DC. No interaction terms were found.

Discussion

This study shows that SS has a large impact on HR-QOL, employment and disability as reflected by lower SF-36 scores and employment rates, and higher disability rates when compared with the general Dutch population. Moreover, analysis of HR-QOL revealed that sSS patients were more limited in physical activities than pSS patients. Although the results are obtained in a Dutch cohort of SS patients, the striking differences in HR-QOL, employment and disability suggest that the results of our study are not limited to the Dutch population, but probably are generally applicable to SS patients when compared with healthy subjects.

Reduced HR-QOL in SS patients compared with normative data has been reported before, but these studies were performed in smaller populations.(6;9;12;15) Overall, the SF-36 scores for pSS patients in our study were comparable to those mentioned in earlier literature. (8-10;15)

We observed more limitations in physical functioning in sSS than in pSS patients. This is in contrast to the results described by Sutcliffe et al. (7) and Tensing et al.(9) The latter studies were performed in smaller patient cohorts and mainly included sSS patients with SLE as second autoimmune disease. The associated rheumatic disease in our sSS patients was more diverse (RA, SLE and other). RA patients are considered to be more restricted in physical functioning than SLE patients (16), which might explain the difference in results. We, however, did not observe such a difference between sSS/RA and sSS/SLE patients; perhaps because of the relatively small sSS subgroups in our study.

In our regression analyses several demographic and clinical factors were found to be associated with HR-QOL. The unexplained variance probably reflects unmeasured, non-disease related psychosocial factors such as self-esteem, support and coping strategies (17), and other factors such as immunologic parameters, delay in diagnosis and untreated or undiagnosed depression.(15) Interestingly, fatigue was an important explanatory variable for reduced physical and mental HR-QOL. (5;9;18)This finding is in agreement with other studies. Furthermore, the importance of fatigue in SS was underscored by the fact that the majority of SS patients felt tired and 40% ranked fatigue as their most severe symptom. Fatigue should therefore be considered as an important treatment target.

Segal et al.(19) demonstrated that psychological variables such as depression are determinants for fatigue, but only partly account for it. Since depression could be of importance for our outcome measures as well, the use of antidepressants was scored in our population (9%). The regression analyses showed that antidepressants were a predictive factor for mental HR-QOL, as can be expected; but not for physical HR-QOL, employment or receiving DC.

We observed low employment and high disability rates in SS, which also have been reported for rheumatic diseases such as RA (17;20) and ankylosing spondylitis.(17) To our knowledge, these results have not previously been reported in SS patients.

A high level of education and comorbidity were the most significant predictors for having paid employment. One would expect, however, that fatigue and arthralgia would also have influenced the employment status. A possible explanation for the lack of this association could be that, with time, patients have gradually adapted their activities to these symptoms. This hypothesis is supported by the fact that only 10% of employed patients had a full-time job.

We found a higher frequency of EGM (95%) compared with other studies.(8;12;15) This can partly be explained by the extended definition of EGM used in this study. Interestingly,

Table 3 Linear multivariate regression analyses for the PCS and MCS of the SF-36.

PCS, model 1			**PCS, adjusted for confounding**		
Variable	***ß [95% CI]***	***P***	**Variable**	***ß [95% CI]***	***P***
Fatigue	-24.26 [-33.07 – -15.44]	0.000	Fatigue	-21.38 [-30.31 – -12.46]	0.000
Tendomyalgia	-9.18 [-15.22 – -3.13]	0.003	Tendomyalgia	-7.62 [-14.22 – -1.03]	0.024
Comorbidity	-18.51 [-24.97 – -12.06]	0.000	Comorbidity	-17.97 [-25.11 – -10.82]	0.000
			Male sex	-11.38 [-22.11 – -0.65]	0.038
			Receiving DC	-10.71 [-17.13 – -4.29]	0.001
Male sex	-12.69 [-23.47 – -1.92]	0.021	Disease duration (years)	0.15 [-0.27 – 0.56]	0.487
Receiving DC	-9.64 [-15.95 – -3.34]	0.003	NSAID use	-4.37 [-11.67 – 2.94]	0.239
			Antidepressant use	-6.76 [-18.19 – 4.67]	0.244
			Employment	-0.95 [-2.31 – 1.14]	0.217
MCS, model 1			**MCS, adjusted for confounding**		
Variable	***ß [95% CI]***	***P***	**Variable**	***ß [95% CI]***	***P***
Fatigue	-15.97 [-24.48 – -7.45]	0.000	Fatigue	-16.92 [-26.26 – -7.57]	0.000
Dry mouth	17.93 [5.94 – 29.91]	0.004	Dry mouth	16.75 [2.50 – 31.00]	0.022
Articular involvement	-7.63 [-13.65 – -1.60]	0.008	Articular involvement	-5.48 [-12.18 – 1.22]	0.108
Artificial saliva use	-9.33 [-18.46 – -0.21]	0.045	Artificial saliva use	-12.58 [-22.97 – -2.20]-	0.018
Antidepressant use	-9.57 [-20.47 – 1.32]	0.085	Antidepressant use	-11.32 [-24.18 – 1.54]	0.084
Comorbidity	-9.49 [-15.74 – -3.23]	0.003	Comorbidity	-11.91 [-18.92 – -4.89]	0.001
			Receiving DC	-2.11 [-8.68 – 4.45]	0.526

PCS = physical component summary score; MCS = mental component summary score; *ß* = regressioncoeficient; 95% CI = 95% confidence interval; DC = disability compensation; NSAIDs = non-steroidal anti-inflammatory drugs.

Table 4 Education level, employment characteristics and disability compensation (DC) in SS patients of working age.

Employment characteristics (n,%)	GDP n=135	SS patients n=135	*P SS patients vs GDP*	pSS patients n=109	sSS patients n=26	*P* pSS vs sSS
Level of education						
Low	31 (23.5%)	5 (3.7%)	<0.001	5 (3.8%)	0	0.800
Middle	57 (43.2%)	94 (69.6%)		75 (57.7%)	19 (57.6%)	
High	44 (33.3%)	33 (24.4%)		26 (20.0%)	7 (21.2%)	
Unknown		3 (2.2%)		3 (2.3%)	0	
Paid employment	109 (82.6%)	69 (51.1%)	<0.001	58 (53.2%)	11 (42.3%)	0.297
Full time paid job	26 (23.9%)	7 (10.1%)	<0.01	7 (12.1%)	0	0.237
Hours worked per week (mean±SD)	26.9±14.2	21.7±11.6	0.011	21.7±12.1	21.3±8.5	0.914
Days sick leave per year (mean±SD)	NA	15.6±39.0	NA	14.7±37.8	22.3±50.0	0.675
Receiving DC	2 (1.5%)	63 (46.7%)	<0.001	49 (45.0%)	14 (53.8%)	0.267
Full DC	NA	28 (44.4%)	NA	21(42.9%)	7 (50.0%)	0.434
Disability percentage (mean±SD)	NA	66.2±30.2	NA	63.6±30.0	75.8±30.0	0.246
Cause receiving DC						
pSS, sSS or associated rheumatic disease	NA	41 (65.1%)	NA	33 (67.3%)	8 (57.1 %)	
Other		7 (11.1%)		6 (12.2%)	1(7.1%)	
Unknown		15 (23.8%)		10 (20.4%)	5 (35.7%)	

GDP = general Dutch population; n = number of patients; DC = disability compensation; NA = not available.

we found a higher frequency of Raynaud's phenomenon (43%), as compared with the study performed by García-Carrasco et al. (16%).(12) This may be explained by different weather circumstances in The Netherlands. The observed higher prevalence of lymphoproliferative disease (15% vs. 2%) may be related to the use of parotid gland biopsies in the diagnostic work-up of our patients.(21) Parotid biopsies are more suited for (early) detection of lymphoproliferative disease than labial biopsies as mucosa associated lymphoid tissue (MALT) and non-Hodgkin lymphomas are rarely found in labial glands.

Although the percentage of patients with EGM did not differ between pSS and sSS patients, it should be noted that part of the EGM in sSS patients could be attributed to the associated autoimmune disease and not only to SS. EGM and EGM related treatment were predictive for HR-QOL, employment and receiving DC. Therefore, there is a need for accurate follow-up and treatment aimed at EGM.

The response rate of 83% in our study is very reasonable. As such, the risk of a sampling bias of certain categories of patients to be preferentially included in this study is considered negligible. Furthermore, we did not observe any significant differences for age, sex and pSS/sSS ratio between responders and non-responders. We, therefore, conclude that our results are representative for SS patients regularly attending a Medical Center specialized in SS patient care.

Table 5 Logistic multivariate regression analyses for employment and receiving disability compensation (DC) in SS patients.

Employment, model 1			**Employment, adjusted for confounding**		
Variable	***Odds ratio [95% CI]***	***P***	**Variable**	***Odds ratio [95% CI]***	***P***
Bladder involvement	0.19 [0.05 – 0.75]	0.017	Bladder involvement	0.20 [0.05 – 0.81]	0.024
Oral moisturising gel use	0.32 [0.11 – 0.94]	0.038	Oral moisturising gel use	0.37 [0.12 – 1.15]	0.084
NSAID use	0.30 [0.12 – 0.81]	0.017	NSAID use	0.25 [0.09 – 0.70]	0.008
Oral corticosteroids use	0.16 [0.04 – 0.59]	0.006	Oral corticosteroids use	0.14 [0.04 – 0.56]	0.005
Comorbidity	0.13 [0.05 – 0.36]	0.000	Comorbidity	0.14 [0.05 – 0.39]	0.000
Age at diagnosis (years)	0.95 [0.92 – 0.97]	0.000	Age at diagnosis	0.97 [0.92 – 1.02]	0.261
High level of education	4.39 [1.69 – 11.44]	0.002	High level of education	4.21 [1.59 – 11.16]	0.004
			Autoimmune thyroiditis	0.46 [0.09 – 2.54]	0.376
			Artificial tears use	0.50 [0.18 – 1.37]	0.177
			Age	0.97 [0.92 – 1.02]	0.250
Receiving DC, model 1			**Receiving DC, adjusted for confounding**		
Variable	***Odds ratio [95% CI]***	***P***	**Variable**	***Odds ratio [95% CI]***	***P***
Number of EGM	1.37 [1.04 – 1.80]	0.026	Number of EGM	1.28 [0.96 – 1.70]	0.099
Artificial saliva use	6.89 [1.92 – 24.76]	0.003	Artificial saliva use	6.21 [1.66 – 23.18]	0.007
Antimalarial drug use	3.41[1.19 – 9.74]	0.022	Antimalarial drug use	2.79 [0.94 – 8.32]	0.065
Comorbidity	2.70 [1.08 – 6.79]	0.034	Comorbidity	2.73 [1.05 – 7.11]	0.039
Age at diagnosis (years)	0.93 [0.90 – 0.97]	0.000	Age at diagnosis (years)	0.94 [0.90 – 0.97]	0.000
Male sex	23.11 [4.40 – 121.24]	0.000	Male sex	32.21 [5.23- 198.42]	0.000
High level of education	2.86 [1.09 – 7.50]	0.032	High level of education	2.66 [1.00 – 7.06]	0.050
			Fatigue	3.33 [0.67 – 16.57]	0.142
			Skin involvement other than cutaneous vasculitis	1.35 [0.41 – 4.42]	0.625
			Pilocarpine use	2.72 [0.76 – 9.74]	0.124

95% CI = 95% confidence interval; UTI = urinary tract infections; NSAIDs = non-steroidal anti-inflammatory drugs; EGM = extraglandular manifestations.

Since many SS patients suffer from reduced HR-QOL and are restricted in social and work related activities, there is a great need for developing adequate treatment modalities to reduce SS related complaints and to intervene in the progression of SS. Currently, no causal systemic treatment is available in SS and, therefore, only symptomatic treatment can be given. Recently, some studies reported good results of treatment with biologicals, especially anti-CD20 treatment.(22-25) Therefore, further development and evaluation of systemic treatment options should be stimulated.

Conclusion

SS has a large impact on HR-QOL, employment and disability as reflected by lower SF-36 scores and employment rates, and higher disability rates in SS patients as compared with the general Dutch population. Several demographical and clinical factors were associated with HR-QOL, employment and receiving disability compensation. Physical functioning, bodily pain and general health were worse in sSS than in pSS patients.

Acknowledgements

We would like to thank Dr. M. Pompen and Dr. E. Ten Vergert for their expertise in the development of the questionnaire and Dr. M. Jalving for reading the manuscript and providing constructive criticism. Also we would like to thank Prof. N.K. Aaronson and Mr. C.M. Gundy of the Netherlands Cancer Institute and the Dutch Office of Statistics, for providing us with age and sex matched normative data on HR-QOL, employment and DC. For their assistance in analysing the data, we are gratefully to J. Bulthuis-Kuiper and R.P.E. Pollard.

Reference List

(1) Hansen A, Lipsky PE, Dorner T. Immunopathogenesis of primary Sjögren's syndrome: implications for disease management and therapy. Curr Opin Rheumatol 2005; 17(5):558-65.

(2) Fox RI. Sjögren's syndrome. Lancet 2005; 366(9482):321-31.

(3) Mitsias DI, Kapsogeorgou EK, Moutsopoulos HM. Sjogren's syndrome: why autoimmune epithelitis? Oral Dis 2006; 12(6):523-32.

(4) Boonen A, Rasker JJ, Stucki G. The international classification for functioning, disability and health. A challenge and a need for rheumatology. Clin Rheumatol 2007; 26(11):1803-8.

(5) Bjerrum K, Prause JU. Primary Sjögren's syndrome: a subjective description of the disease. Clin Exp Rheumatol 1990; 8(3):283-8.

(6) Strombeck B, Ekdahl C, Manthorpe R, Wikstrom I, Jacobsson L. Health-related quality of life in primary Sjogren's syndrome, rheumatoid arthritis and fibromyalgia compared to normal population data using SF-36. Scand J Rheumatol 2000; 29(1):20-8.

(7) Sutcliffe N, Stoll T, Pyke S, Isenberg DA. Functional disability and end organ damage in patients with systemic lupus erythematosus (SLE), SLE and Sjögren's syndrome (SS), and primary SS. J Rheumatol 1998; 25(1):63-8.

(8) Champey J, Corruble E, Gottenberg JE, Buhl C, Meyer T, Caudmont C et al. Quality of life and psychological status in patients with primary Sjögren's syndrome and sicca symptoms without autoimmune features. Arthritis Rheum 2006; 55(3):451-7.

(9) Tensing EK, Solovieva SA, Tervahartiala T, Nordstrom DC, Laine M, Niissalo S et al. Fatigue and health profile in sicca syndrome of Sjögren's and non-Sjögren's syndrome origin. Clin Exp Rheumatol 2001; 19(3):313-6.

(10) Bowman SJ, Booth DA, Platts RG. Measurement of fatigue and discomfort in primary Sjögren's syndrome using a new questionnaire tool. Rheumatology (Oxford) 2004; 43(6):758-64.

(11) Vitali C, Bombardieri S, Jonsson R, Moutsopoulos HM, Alexander EL, Carsons SE et al. Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. Ann Rheum Dis 2002; 61(6):554-8.

(12) Garcia-Carrasco M, Ramos-Casals M, Rosas J, Pallares L, Calvo-Alen J, Cervera R et al. Primary Sjögren's syndrome: clinical and immunologic disease patterns in a cohort of 400 patients. Medicine (Baltimore) 2002; 81(4):270-80.

(13) Ramos-Casals M, Font J, Garcia-Carrasco M, Brito MP, Rosas J, Calvo-Alen J et al. Primary Sjögren's syndrome: hematologic patterns of disease expression. Medicine (Baltimore) 2002; 81(4):281-92.

(14) Aaronson NK, Muller M, Cohen PD, Essink-Bot ML, Fekkes M, Sanderman R et al. Translation, validation, and norming of the Dutch language version of the SF-36 Health Survey in community and chronic disease populations. J Clin Epidemiol 1998; 51(11):1055-68.

(15) Belenguer R, Ramos-Casals M, Brito-Zeron P, del Pino J, Sentis J, Aguilo S et al. Influence of clinical and immunological parameters on the health-related quality of life of patients with primary Sjögren's syndrome. Clin Exp Rheumatol 2005; 23(3):351-6.

(16) Benitha R, Tikly M. Functional disability and health-related quality of life in South Africans with rheumatoid arthritis and systemic lupus erythematosus. Clin Rheumatol 2007; 26(1):24-9.

(17) Chorus AM, Miedema HS, Boonen A, Van Der Linden S. Quality of life and work in patients with rheumatoid arthritis and ankylosing spondylitis of working age. Ann Rheum Dis 2003; 62(12):1178-84.

(18) Barendregt PJ, Visser MR, Smets EM, Tulen JH, van den Meiracker AH, Boomsma F et al. Fatigue in primary Sjögren's syndrome. Ann Rheum Dis 1998; 57(5):291-5.

(19) Segal B, Thomas W, Rogers T, Leon JM, Hughes P, Patel D et al. Prevalence, severity, and predictors of fatigue in subjects with primary Sjögren's syndrome. Arthritis Rheum 2008; 59(12):1780-7.

(20) Verstappen SM, Boonen A, Bijlsma JW, Buskens E, Verkleij H, Schenk Y et al. Working status among Dutch patients with rheumatoid arthritis: work disability and working conditions. Rheumatology (Oxford) 2005; 44(2):202-6.
(21) Pijpe J, Kalk WWI, van der Wal JE, Vissink A, Kluin PM, Roodenburg JLN et al. Parotid gland biopsy compared with labial biopsy in the diagnosis of patients with primary Sjögren's syndrome. Rheumatology (Oxford) 2007; 46(2):335-41.
(22) Devauchelle-Pensec V, Pennec Y, Morvan J, Pers JO, Daridon C, Jousse-Joulin S et al. Improvement of Sjögren's syndrome after two infusions of rituximab (anti-CD20). Arthritis Rheum 2007; 57(2):310-7.
(23) Meijer JM, Pijpe J, Bootsma H, Vissink A, Kallenberg CG. The future of biologic agents in the treatment of Sjögren's syndrome. Clin Rev Allergy Immunol 2007; 32(3):292-7.
(24) Pijpe J, van Imhoff GW, Vissink A, van der Wal JE, Kluin PM, Spijkervet FK et al. Changes in salivary gland immunohistology and function after rituximab monotherapy in a patient with Sjögren's syndrome and associated MALT lymphoma. Ann Rheum Dis 2005; 64(6):958-60.
(25) Pijpe J, van Imhoff GW, Spijkervet FKL, Roodenburg JLN, Wolbink GJ, Mansour K et al. Rituximab treatment in patients with primary Sjögren's syndrome: An open-label phase II study. Arthritis Rheum 2005; 52(9):2740-50.